REMARKS/ARGUMENTS

**Claims**

35 USC § 103(a) Rejection of Claims 11, 12, 15, 16 and 25

The Office Action rejected Claims 11, 12, 15, 16 and 25 under 35 USC 103(a) as being obvious over Lambright *et al.* 1999; Morrison *et al.* 1994, and Kirn *et al.* 2001; and various combinations of other references.

The Applicants disagree with the conclusion of the Office Action that the various combinations of references disclose each and every feature of amended Claims 11, 12, 15, 16 and 25.

Claim 25 has been amended to more clearly claim the disclosed method. Claim 25 now includes the feature "wherein the carrier cell is selected from the group consisting of (1) A549 cell and (2) mixture of A549 cell and 293 cell".

Although Lambright discloses oncolytic therapy using HSV retrovirus infected LLC cells as a carrier cell, it does not teach the step of administrating a non-proliferative virus for immunological treatment and producing an oncolytic virus infected carrier cell by using the same type of virus as the virus for immunological treatment. In fact, Lambright discloses that "(H)SV-1716 may provide an oncolytic therapy for lung cancer even in the absence of immune system induction and..." (*see*, for example, page 1756, right column, second paragraph or page 1760, left column, second paragraph). Furthermore, Lambright discloses using LLC cell as carrier cell but does not teach using A549 cell or mixture of A549 cell and 293 cell as carrier cell.

Additionally, even though Morrison discloses the immunization of a subject using a non-proliferative virus, i.e. HSV-1, Morrison does not disclose its use in a method for cancer gene therapy using a non-proliferative virus for immunological treatment and a specific carrier cell. Morrison *et al.* disclosure to immunize a subject against HSV-1 mediated ocular infection and disease would not accomplish the presently claimed method, so Morrison's method would not inherently give the same result.

The Examiner also asserts that the present invention is obvious to one skilled in the art, because all the claimed elements are known in the prior art and that an artisan would be motivated to combine the steps of the present invention because at the time of the instant

invention those skilled in the art recognized the problems for the development of a virotherapy platform for the treatment of cancer and knew a balance between viral replication and induction of the host immune response will be essential for this therapy to be effective, by Kirn *et al.*

Applicants believe this assertion is hindsight and it would not be obvious to try this combination. Even though Kirn mentions the issues of virotherapy for treatment of cancer; Lambright does not disclose the step of administrating a non-proliferative virus for immunological treatment to induce a Cytotoxic T lymphocytes (CTL) reaction prior to a carrier cell and then administrating a specific carrier cell which is infected by the same type of virus as the virus for immunological treatment; and it is not obvious to try to combine Morrison, which relates to an ocular infection, with Lambright in order to achieve the presently claimed method.

Moreover, the method as defined in amended claim 25 can achieve a distinctly strong antitumor effect. As shown in Fig. 18 (a) and (b) of Example 6, a stronger *in vivo* antitumor effect and a far better survival rate were obtained when administrating oncolytic virus infected carrier cell (A549 cell) after oncolytic virus for immunological treatment compared to those obtained when administrating carrier cell alone or virus alone. Additionally, it is shown that the combined use of A549 and 293 cells as carrier cells, as presently claimed, also achieved a strong antitumor effect. The strong synergetic effect achieved by using a specific carrier cell and a non-proliferative virus in combination is unpredictable and non-obvious to a skilled artisan.

Therefore the presently claimed method of amended Claim 25 is unobvious over Lambright *et al.* in view of Morrison *et al.* and Kirn *et al.* Claims 11 and 12 are dependent from Claim 25 and thus are also unobvious over the cited references.

The Examiner is requested to remove the combination of Lambright *et al.* 1999; Morrison *et al.* 1994, and Kirn *et al.* 2001, and the various other combinations of references as 103(a) Prior Art references. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 11, 12, 15, 16 and 25.

35 USC § 103(a) Rejection of Claims 2, 5, 6 and 24

The Office Action rejected Claims 2, 5, 6 and 24 under 35 USC 103(a) as being obvious over Lambright *et al.* 1999; Molnar-Kimber *et al.*, and Kirn *et al.* 2001; and various combinations of other references.

The Applicants disagree with the conclusion of the Office Action that the various combinations of references disclose each and every feature of amended Claims 2, 5, 6 and 24.

Claim 24 has been amended to more clearly claim the disclosed kit. Claim 24 now includes the feature "wherein the carrier cell is selected from the group consisting of (1) A549 cell and (2) mixture of A549 cell and 293 cell".

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to package the non-proliferative virus for immunological treatment, the carrier cell and the oncolytic virus in a kit since one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions in view of the cited references.

However, Lambright *et al.*, Kirn *et al.* and Molnar-Kimber *et al.* do not disclose using a non-proliferative virus with a specific carrier cell such as A549 cell or mixture of A549 cell and 293 cell. Although Morrison *et al.* and Inglis *et al.* disclose a non-proliferative virus and inactivated virus for immunological treatment, Morrison *et al.* relates to an ocular infection and Inglis *et al.* relates to HSV infection, respectively, and both references do not disclose a cancer gene therapy. Therefore, applicants contend that it would not be obvious to try the combination of Morrison *et al.* and Inglis *et al.* with Lambright *et al.*, Kirn *et al.* and Molnar-Kimber *et al.* in order to achieve the presently claimed drug kit.

In addition, as described above, the strong antitumor effect achieved by using a non-proliferative virus for immunological treatment in combination with oncolytic virus (same type of virus as the virus for immunological treatment) infected carrier cell (A549 cell or mixture of A549 cell and 293 cell) is demonstrated by Example 6 (especially in Fig 18 and Fig 25) of the present specification; and this remarkable effect is not predictable by one skilled in the art.

As for using A549 cell as a carrier cell, the Examiner points out that Harrison *et al.* teaches the use of A549 cells to produce oncolytic adenoviruses in a method to treat tumors. Harrison *et al.* only discloses that A549 cells can be used in the production of a tumor model mouse, but does not even mention that A549 cell can be used as a carrier cell in the treatment of tumors.

Therefore, applicants state the presently claimed kit as in amended Claim 24 is unobvious over Lambright *et al.* in view of Morrison *et al.* and Kirn *et al.*, and in further view of Molnar-Kimber *et al.*, Inglis *et al.* and Harrison *et al.* Claims 4 and 21 are canceled; and Claims 2, 5 and 6 depend on Claim 24 and thus these claims are also unobvious over cited references.

The Examiner is requested to remove the combination of Lambright *et al.* in view of Morrison *et al.* and Kirn *et al.*, and in further view of Molnar-Kimber *et al.*, Inglis *et al.* and Harrison *et al.* as 103(a) Prior Art references. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 2, 5, 6 and 24.

Rejoinder of Claims 7 – 9, 13, 14 and 17 –19

Claims 7 – 9, 13, 14 and 17 –19 are currently withdrawn. As Claims 24 and 25 are allowable as written and Claims 7 – 9, 13, 14 and 17 –19 contain all the features of these claims of which they depend, the Examiner is respectfully requested to rejoin Claims 7 – 9, 13, 14 and 17 –19. In light of the foregoing arguments, the Examiner is respectfully requested to allow Claims 7 – 9, 13, 14 and 17 –19.

No Disclaimers or Disavowals

Although the present communication may include alterations to the claims, the Applicants are not conceding in this application that previously pending claims are not patentable. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Conclusion

Claims 2, 5 – 9, 11 – 19, 24 and 25 are pending. Claims 24 and 25 are Currently amended. Claims 2, 5, 11, 12, 15 and 16 are Previously presented. Claims 7 – 9, 13, 14 and 17 – 19 are Withdrawn. Claims 1, 3, 4, 10 and 20 – 23 are Canceled.

No additional fees are believed due; however, the Commissioner is authorized to charge any additional fees now and in the future which may be due, including any fees for additional extension of time, or credit overpayment to credit card information.

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